International Journal of Surgery Case Reports 25 (2016) 4–6

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

Marginal zone lymphoma of the breast—A diminished role for surgery

Suman B. Koganti (MD)*, Alejandra Lozada (MD), Ernesto Curras (MD), Ajay Shah (MD, FACS)

Bronx-Lebanon Hospital Center, Icahn School of Medicine at Mount Sinai, 1650 Grand Concourse, NY 10457, USA

ARTICLE INFO

Article history:
Received 17 May 2016
Accepted 25 May 2016
Available online 2 June 2016

Keywords:
MZL—marginal zone lymphoma
AJCC—American joint commission on cancer
TNM— tumor, node, metastasis
PBL—primary breast lymphoma

ABSTRACT

INTRODUCTION: Primary breast lymphoma by definition is localized to one or both the breasts with or without involvement of regional lymph nodes with no other extra mammary site involvement. Role of surgery in the treatment armamentarium is less well defined.

PRESENTATION OF CASE: A 62 year old post-menopausal lady was found to have 1.2 × 1.2 × 0.6 cm mass in the left breast on diagnostic mammography. Core needle biopsy reveals marginal zone lymphoma. Complete staging work-up was performed which was negative for regional spread and metastatic foci. She was diagnosed to have a localized stage IE extra nodal low grade marginal zone lymphoma of the MALT type involving breast. She received radiotherapy to the breast and is in remission at follow up after one year.

DISCUSSION: Accurate diagnosis requires adequate tissue biopsy either by a core needle or a surgical biopsy for histopathologic evaluation and immunophenotyping. Immunohistochemically the tumors are positive for pan B-cell markers (CD 19, CD 20, CD22, and CD 79a) and lack T cell markers. For stage IE Marginal zone lymphoma radiotherapy alone and for stage IIE combined chemo-radiation offers the best possible control of the disease. Progression free survival for MZL is better than diffuse large B-cell lymphoma.

CONCLUSION: At present the best evidence support radiotherapy in localized disease and combined chemo-radiation in advanced disease. Role of surgery is minimal and is seen in case of diagnostic dilemma. Rarity of the diagnosis precludes large scale prospective studies making therapeutic decisions difficult and challenging.

1. Introduction

Marginal zone lymphomas are a group of low grade B-cell lymphomas that arise from the marginal zone of the secondary lymphoid follicles. Three distinct subtypes are mentioned in the most recent 2008 WHO classification (1) Extra nodal marginal zone or MALT lymphomas (2) Splenic marginal zone lymphomas (3) Nodal marginal zone lymphomas [1]. Extra-nodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) type occurs mainly in the gastrointestinal tract but can occur in salivary gland, thyroid, orbit, lung, and breast tissue [2]. Marginal zone lymphomas of the breast is a rare occurrence. Very sparse literature exists to describe the ideal management strategy for these tumors.

1.1. Presentation of case

A 62 year old post-menopausal lady with no significant past medical or family history of breast cancer related malignancies undergoes a routine screening mammogram which reveals new onset nodular densities in the left breast as compared to a normal mammogram a year before (BIRADS 1). Clinical examination does not reveal any palpable breast lesions and cervical, axillary or peripheral lymph nodes elsewhere in the body. She undergoes diagnostic mammography and sonogram which reveals 1.2 × 1.2 × 0.6 cm mass in the left breast. A sonoguided biopsy demonstrates small lymphocytes with abundant cytoplasm and the presence of a lympho-epithelial lesion most consistent with a marginal zone lymphoma.IHC staining was positive for CD20/BCL2 (Fig. 2) and negative for cyclin D1, CD10, CD3 and CD5. MRI of bilateral breasts did not reveal any mass lesions in the contralateral breast and is consistent with mammogram findings (Fig. 1). A complete staging work-up with CT chest, abdomen and pelvis along with whole body PET-CT was performed which was negative for regional spread and metastatic foci. She was diagnosed to have a localized stage IE extra nodal low grade marginal zone lymphoma of the MALT type of breast. She is currently undergoing radiotherapy and is in follow up with oncology and breast clinic and her disease is in remission on follow up imaging at present.

* Corresponding author at: 1650 Selwyn avenue, New York 10457, USA.
E-mail address: skoganti@bronxleb.org (S.B. Koganti).

http://dx.doi.org/10.1016/j.ijscr.2016.05.041

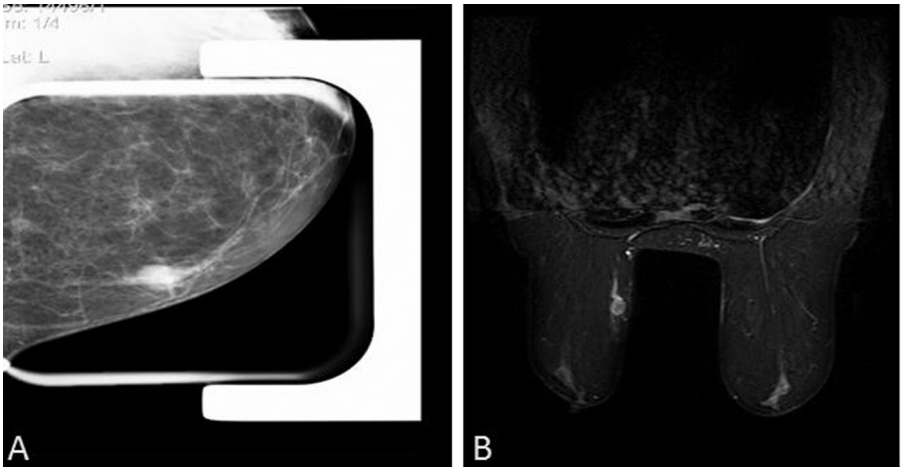

Fig. 1. Panel A: Diagnostic mammogram of left breast cranio-caudal view identified a new onset dominant mass in the left upper inner quadrant (BI-RADS 4) Panel B: short T1 inversion recovery MR images of B/L breast demonstrates suppressed normal breast adiposity in both breasts and a dominant mass with high signal intensity that corresponds to lymphoma.

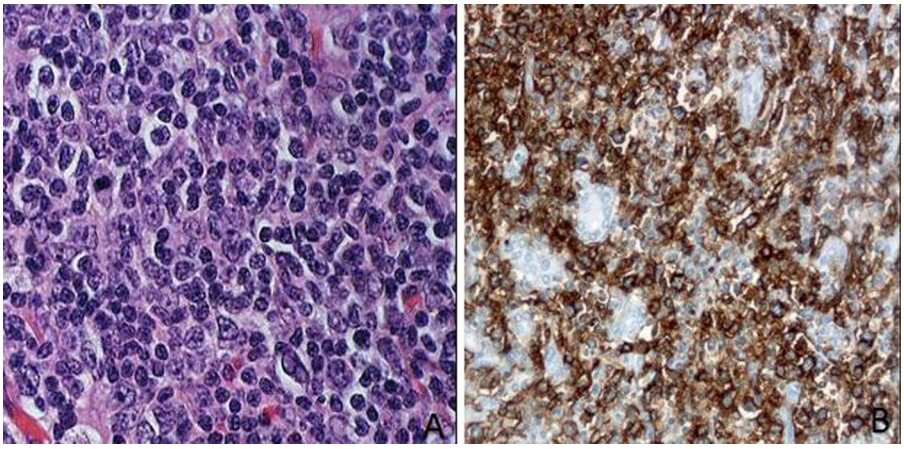

Fig. 2. Panel A: H&E sections revealed aggregates of small lymphocytes and few scattered large lymphoid cells. A few distorted reactive lymphoid follicles also appear. Panel B: IHC studies reveal small lymphocytes show predominant staining for CD20/BCL2 and negative for CD33/CD5/CD10 and cyclinD1. Overall Ki-67 stains approx. 10% of lymphocytes.

2. Discussion

Primary breast lymphoma by definition is localized to one or both the breasts with or without involvement of regional lymph nodes with no other extra mammary site involvement. Criterion standard were defined for primary breast lymphoma by Wiseman and laio in 1972 [3] and confer uniformity in diagnosis, evaluation and treatment of these tumors. Primary breast lymphomas constitute less than 1% of all NHL, 1.7–2.2% of all extra nodal NHL and 0.04–0.5% of all malignant neoplasms of the breast [4,5]. Marginal zone lymphoma constitute approximately 9% of all primary breast lymphomas [6]. Despite being the second most common variant of PBL it is exceedingly rare in occurrence. In the largest multicenter retrospective study (1980–2003) only 24 cases of marginal zone lymphoma were reported [6]. A pathophysiological role of an inciting chronic inflammation or infection like the gastrointestinal MALT lymphomas is not described in breast tissue (Fig. 2).

An enlarging painless breast mass in an elderly patient is the most common presentation. Bilateral presentation is not uncommon. The median age at presentation is 68 years (47–92 yrs) with a higher female predilection. They tend to be larger than epithelial breast cancers, and the average size is 3 cm. Marginal zone lymphomas tend to be low grade tumors with relative absence of advanced disease like respiratory symptoms, bulky lymphadenopathy, “B” symptoms, and central nervous system (CNS) symptoms [6–8]. Most common mammographic features are solitary, uncalcified soft-tissue mass seen in 60–70% of the patients [9]. Sonographic appearance is not specific for any lymphoma. Well defined to poorly defined, hypo- to hyperechoic masses and focal or diffuse involvement with variable attenuation are the main ultrasonographic features [9]. The typical appearance on an MRI is an ill-defined, non-spiculated, hypointense masses in T1W images, which showed rapid and strong enhancement in dynamic sequence. Non-invasive studies are in agreement with final pathological diagnosis nearly 93% of the time [9].

Diagnosis of marginal zone lymphoma is based on cytological and histopathologic features. Fine needle as piration cytology alone is an inadequate study for primary breast lymphoma. Often it becomes difficult to distinguish lymphoid cells from reactive lymphocytes. Adequate tissue biopsy either by a core needle or a surgical biopsy for histopathologic evaluation and immunophenotyping is of paramount importance. Centrocyte (small to medium size lymphocyte with abundant cytoplasm and irregularly shaped nuclei) infiltration, scattered blast cells and lymph-epithelial lesion are pathognomonic of marginal zone lymphoma regardless of the site of origin. Immunohistochemically the tumors are positive for pan B-cell markers (CD 19, CD 20, CD22, and CD 79a) and lack staining for T

cell markers CD5, CD10 and Bcl-1. Clonality and tumorigenesis of marginal zone lymphomas are determined by chromosomal translocations. The translocation t (11; 18) (q21; q21) is found in most anatomical sites and is seen in nearly 50% of the cases. Translocation t(11:18)(q21;q21) is next most common seen in 20% of marginal zone lymphomas but not specific as there is significant overlap from follicular lymphoma subtype. Chromosomal translocations t(1:14)(p22;q32) is rare however more specific for marginal zone lymphoma of the GI tract [2,10,11].

Staging work-up recommended by NCCN for extranodal NHL is no different for any subtype of primary breast lymphomas. At the minimum a careful history and physical, CT chest, abdomen and pelvis, or integrated PET-CT, Bone marrow aspiration and biopsy, and laboratory studies (CBC, Comprehensive metabolic panel) are recommended. Assessment of the contralateral breast is essential since 10% of the lymphomas involve the contralateral breast [12]. Luganos modification of the Ann arbor staging system is used to determine the stage of the extra-nodal lymphoma. Stage IE defines disease limited to breast only and stage IIE involves lesion limited to the breast and ipsilateral lymph nodes. Disease that has metachronous spread beyond the breast with primary breast presentation including bone marrow is included in IIE by expert groups.

Treatement options in primary breast lymphoma are tailored according to the biological behavior of the lymphoma. For aggressive variants like diffuse large B-cell lymphoma systemic therapy (chemotherapy) alone or combined with some kind of local therapy (Radiotherapy or surgery) offers the best survival rates [13]. However for indolent and low grade lymphomas local treatment (radiotherapy or surgery) would suffice. Selection of treatment for marginal zone lymphoma varied widely in literature. In the largest reported IELSG series radiotherapy and surgery either alone or in combination were used in the treatment of nearly 70% of the reported series. Chemotherapy alone or in combination was used in less than 25% of patients. Role of surgery in the treatment of marginal zone lymphoma and lymphomas overall has declined since 1990. Majority of the surgical series with a lumpectomy or quadrentectomy included patients with a pre-operative breast lesion misdiagnosed as a poorly differentiated carcinoma or for obtaining a tissue diagnosis. Outside of these two indications radical surgery is met with inferior survival rates and offers no real advantage [6,13]. Thus for a localized stage IE Marginal zone lymphoma radiotherapy alone and for an advanced lesion stage IIE (involved lymph nodes or discontiguous spread) combined chemo-radiation offers the best possible control of the disease. Prognosis for MZL is comparatively better than Aggressive lymphomas like DLBCL and follicular lymphomas. Progression free survival for MZL of the breast was 72% at 3 years,56% at 5 years and 34% at 10 years, respectively (log-rank test:P = 0.55). The median PFS was 7.3years in MZL.OS for MZL was 100% at 3 years, 92% at 5 years and 64% at 10 years, respectively (log-rank test = 0.04) [6].

3. Conclusion

Marginal zone lymphoma is considered as an indolent lymphoma of the breast. Epidemiological surveys describing clinical features and out-comes do not exist. Principles of diagnosis and staging are no different from lymphomas at other sites. At present best evidence support radiotherapy in localized disease and combined chemo-radiation in advanced disease. Rarity of the diagnosis precludes large scale prospective studies making therapeutic decisions difficult and challenging.

Conflicts of interest

No conflicts of interest.

Funding

All the authors report no financial acknowledgments involved for this case report and declare no potential conflicts of interest.

Consent

Informed consent was given by the patient in a written and verbal form.

Author contribution

Study concept and design: Suman B koganti MD, Ernesto Curras MD, Shah Ajay MD,FACS.

Data collection : Suman B koganti MD, Alejandra Lozada MD.

Data analysis and interpretation: Suman B Koganti MD, Ernesto Curras MD, Ajay Shah MD,FACS.

Writing the paper : Suman B koganti MD.

Guarantor

Dr. Ajay Shah, MD, FACS.

References

[1] 3 [1] S.H. Swerdlow, E. Campo, N.L. Harris, et al., WHO Classification of Tumors of Hematopoietic and Lymphoid Tissues, 4th ed., International Agency for Research on Cancer, Lyon, France, 2008.
[2] M. Seth Cohen, Magdalena Petryk, Mala Varma, S. Peter Kozuch, D. Elizabeth Ames, L. Michael Grossbard, Non-Hodgkin's lymphoma of mucosa-associated lymphoid tissue, Oncologist 11 (10) (2006) 1100–1117.
[3] C. Wiseman, K.T. Liao, Primary lymphoma of the breast, Cancer 29 (1972) 1705–1712.
[4] S.H. Kim, M.P. Ezekiel, R.Y. Kim, Primary lymphoma of the breast, Am. J. Clin. Oncol. 22 (1999) 381–383.
[5] C.M. Shapiro, D. Mansur, Bilateral primary breast lymphoma, Am. J. Clin. Oncol. 24 (2001) 85–86.
[6] G. Martinelli, G. Ryan, J.F. Seymour, L. Nassi, S. Steffanoni, A. Alietti, L. Calabrese, G. Pruneri, L. Santoro, M. Kuper-Hommel, R. Tsang, P.L. Zinzani, A. Taghian, E. Zucca &F. Cavalli, Primary follicular and marginal-zone lymphoma of the breast: clinical features, prognostic factors and outcome: a study by the International Extranodal Lymphoma Study Group, Ann. Oncol. 0 (2009) 1993–1999.
[7] Nina J. Karlin, Comprehensive Management of Benign and Malignant Diseases, 4th ed. 2009, Chapter 17, Breast Lymphoma, 315–320.
[8] Arnold S Freedman MD, Jonathan Friedberg MD, Breast Lymphoma, UpToDate@2016. edited by Daniel F Hayes MD, Rebecca F Connor MD, W. Post, published by UpToDate in Waltham, MA. Topic 791 Version 20.0.Topic last updated: Feb 17, 2016.
[9] Figen Basaran Demirkazık, MR imaging features of breast lymphoma, Eur. J. Radiol. 42 (2002) 62–64.
[10] A. Auer, R.D. Gascoyne, J.M. Connors, F.E. Cotter, T.C. Greiner, W.G. Sanger, D.E. Horsman, t(ll;18)(q21;q21) is the most common translocation in MALT lymphomass, Ann. Oncol. 8 (October (10)) (1997) 979–985.
[11] G. Ott, T. Katzenberger, A. Greiner, J. Kalla, A. Rosenwald, U. Heinrich, M.M. Ott, H.K. Müller-Hermelink, The t(11;18)(q21;q21) chromosome translocation is a frequent and specific aberration in low-grade but not high-grade malignant non-Hodgkin's lymphomas of the mucosa-associated lymphoid tissue (MALT-) type, Cancer Res. 57 (September (18)) (1997) 3944–3948.
[12] Non-Hodgkin's Lymphomas. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Version 3.2016 @ NCCN.org. (https://www.nccn.org/professionals/physician_gls/pdf/nhl.pdf).
[13] William C. Jennings, Randal S. Baker, Sunshine S. Murray, C. Anthony Howard, Donald E. Parker, Linda F. Peabody, Heather M. Vice, William W. Sheehan, Thomas A. Broughan, Primary Breast lymphoma the role of mastectomy and the importance of lymph node status, Ann. Surg. 245 (5) (2007).